REMARKS/ARGUMENTS

Favorable reconsideration of this application in light of the following discussion is respectfully requested.

Claims 1-6 and 9-15 are pending in this application. Claims 1, 9, and 10 are herein amended. Support for the amendment of claims 1 and 9 is found at least in the specification at page 16, line 20 through page 17, line 9. Support for the amendment of claim 9 is found at least in the original claims. No new matter is added.

In the outstanding Office Action, claims 1, 4, and 5 were rejected under 35 U.S.C. § 103(a) as obvious over Kurihari (US 2002/0155619) in view of Gaillon (WO 99/27349). Claim 2 was rejected as obvious over Kurihari, in view of Gaillon and Bannerjee (US 6,307,630). Claim 6 was rejected as obvious over Kurihari, in view of Gaillon and Bell (US 5,814,277). Claims 9 and 10 were rejected as obvious over Bannerjee, in view of Gaillon.

Claims 1, 4, and 5 were rejected as obvious over Kurihari in view of Gaillon. As amended, claim 1, from which claims 4 and 5 depend, is directed to an automated and robotized platform including a battery of micro-fermentors with a useful culture volume ranging from 2 mL to 500 mL. Each of micro-fermentors includes a cell culture. The platform includes an external sensor for measuring at least an optical property of each cell culture contained in each micro-fermentor. Each platform further includes a mobile sensor holder able to receive the external sensor. The sensor holder has sensor moving means for moving the external sensor from a micr-fermentor to another one and for allowing for the real time measurement of at least one optical property. The platform also has monitoring and processing means for receiving in real time measurements of the optical property from the external sensor and monitoring in real time a movement of the mobile sensor holder. And the platform has a system for regulating a temperature consisting of a Peltier effect autonomous

regulating system. The regulation of the temperature by the Peltier effect is independent and programmable for each micro-fermenter.

The claimed invention relates to an automated and robotized platform for monitoring and regulating cell cultures contained within a micro-fermentor battery. The main object of the instant invention is to provide a platform for cell cultures and a method for measuring the optical properties of cell cultures, which does not have the disadvantages of previously known devices and methods in the same technical field. With the combined features of the present invention, optimal cell culture conditions result, because the device includes a system for measuring the optical properties of the cell culture contained in each micro-fermentor, independent programmable regulation of the temperature for each micro-fermentor. These features allow for the precise tuning of the cell culture conditions. The measurement of the optical properties of each cell culture allows for the determination of essential parameters like cell culture growth or the amount of production of a protein of interest. The independent temperature regulation of each micro-fermentor allows for the appropriate adaptation of the culture conditions , such as required for optimal cell growth or optimal protein production, as the regulation of the growth temperature is an essential parameter in performing a microbial culture. *See* Specification, page 16, lines 21-22. Moreover, the capability of programming the culture temperatures is key to optimizing bacteriological methods. *See* Specification, page 17, lines 1-2.

The cited references do not teach or suggest the claimed invention. Kurihara discloses a fluorescent detection system for performing analysis in the field of clinical diagnosis wherein enzymatic reactions are performed and associated with the generation of a fluorescent reaction product caused by the said enzymatic reaction which occurs. *See* Kurihara, pars. [001]-[002]. The Kurihara invention aims at overcoming the drawbacks of the prior art technical means that were designed for ensuring darkness of the sample when

performing the analysis of a fluorescent signal generated during an enzymatic reaction, which prior art means included notably, specific dark chambers equipped with covers or caps preventing external light to disturb the fluorescence detection and quantification. According to Kurihara, the use of shade covers for covering the entire system or all samples known in the art may be avoided by layering a shielding liquid on the liquid sample to be analyzed. The shielding liquid is unmixable with the liquid sample to be analyzed, in order to prevent external light from entering through the sample container opening. The shielding liquid may be made of oil with a shielding agent added thereto, including a shielding liquid made of carbon black. *See* Kurihara, pars. [0013] to [0016].

The Kurihara device and the method are exclusively aimed at detecting a fluorescent signal generated during an enzymatic reaction. Thus, "the amount of samples is as small as tens μL". *See* Kurihara, par. [0047]. Moreover, the Kurihara device and method are designed to perform fluorescence analysis of a plurality of test samples during or after a single kind of enzymatic reaction. As such, the Kurihara device comprises a single thermostatic unit for controllably setting samples at the designed temperature. Particularly, the Kurihara device "utilizes a single heater 9a and a single temperature sensor 9b". With this arrangement, "it is possible to controllably set samples at a designed temperature by heat-conduction from the sample holder". *See* Kurihara, pars. [0055]-[0056].

In addition, Kurihara teaches that "in order that the samples, which are subjected to the temperature control by the thermostatic unit are insulated from an external temperature to carry out temperature control with higher accuracy, it is preferable to provide the heat-insulated enclosure". In the device of Kurihara, "one embodiment is to accommodate at least the sample holder in a constant temperature enclosure having a constant temperature therein to control the temperature of the sample holder by convection..." *See* Kurihara, par. [0058]. Still further, Kurihara expressly teaches that, due to the combined means of the device that

they disclose, "it becomes possible to carry out incubation, such as enzymatic reaction, for many samples at a desired temperature..." *See* Kurihara, par. [0059]. Finally, Kurihara expressly teaches that "the sample holder has had **a** heater 9a affixed to an outer peripheral portion thereof and **a** temperature sensor 9b provided therein" a specific embodiment of **the** heater consists of "a tape-shaped heater" (see [0071], page 6, beginning of the right column of Kurihara et al.).

It flows from the above description that the device disclosed by Kurihara is specifically designed for fluorescence signal detection/quantification of fluorescent compounds generated following an enzymatic reaction occurring in small volumes (ten μL) samples, which explains why, notably, there is no requirement in the device of Kurihara of any complex heating system, but only of a single heater ensuring the setting of the whole sample holder at the appropriate enzymatic reaction temperature for all samples contained therein.

Gaillon discloses an apparatus and method for measuring optical properties of a sample, including turbidity, by a specific system of feedback control. Gaillon has several disadvantages that are overcome by the present invention. Among the disadvantages are the presence of a plurality of sensors which required individual calibration before use, which led to light measure discrepancies. *See* Specification, page 8, lines 4-29. Gaillon is exclusively aimed at designing a specific feedback control for an optimal optical measurement of the samples to be analyzed. Thus, there is no specific disclosure of a specific heating system.

A claimed invention can only be found obvious if there is "some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *KSR Int'l v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) (*quoting In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006). Moreover, every word in a claim must be considered in determining the question of patentability against the prior art. *In re Wilson*, 424 F.2d 1382, 1385 (CCPA 1970). As

presently claimed, the invention encompasses a feature allowing for the regulation of the temperature by the Peltier effect which is independent and programmable for each micro-fermenter. One skilled in the art would understand Kurihara to not teach such a feature. Disclosing no heating system, Gaillon can not overcome the deficiencies of Kurihara. There can be no combination of the two references to reach the invention of claim 1 or the claims depending therefrom. Applicants respectfully request withdrawal of this rejection.

Claim 2 was rejected as obvious over Kurihari, in view of Gaillon and Bannerjee. Claim 2 depends from claim 1 and includes all of its limitations. As noted above, the combination of Kurihara and Gaillon cannot render claim 1 obvious at least because they do not teach or suggest the regulation of the temperature by the Peltier effect which is independent and programmable for each micro-fermenter. Bannerjee does not remedy the deficiency of this combination. Bannerjee discloses a turbidimeter array system, including (in Figs. 5 and 9) a single external sensor affixed on a mobile sensor holder, in which the sensor system is capable of moving from one sample to be tested to the next sample. Because the turbidimeter device of Bannerjee is exclusively aimed at measuring turbidity from water samples previously collected from a water treatment plant, there is strictly no requirement for any heat regulation system. Thus, Bannerjee does not add any useful teachings to those of Kurihara and Gaillon. Accordingly, the combination of the three references cannot render the claimed invention obvious. Applicants respectfully request withdrawal of this rejection.

Claim 6 was rejected as obvious over Kurihari, in view of Gaillon and Bell. Claim 6 depends from claim 1. Bell relates to an automatic multiple-sample chemical analyzer. The device disclosed by Bell is suitable exclusively for performing chemical reactions and in no way for performing cell cultures. Accordingly, Bell cannot remedy the deficiencies of the earlier combination. The cited references do not teach or suggest the claimed invention, at least because they do not teach or suggest the regulation of the temperature by the Peltier

effect which is independent and programmable for each micro-fermenter. Applicants respectfully request withdrawal of this rejection.

Claims 9 and 10 were rejected as obvious over Bannerjee, in view of Gaillon. Claim 9 (from which claim 10 depends) is directed to a method for automatically measuring at least one optical property of cell cultures contained within a micro-fermentor having a useful culture volume ranging from 2 mL to 500 mL battery wherein the temperature of each micro-fermentor is independently programmable and regulated by Peltier effect. As noted above, neither Bannerjee, nor Gaillon teach or suggest the regulation of the temperature by the Peltier effect which is independent and programmable for each micro-fermenter. Failing to do so, they cannot render claims 9 and 10 obvious. Applicants respectfully request withdrawal of this rejection.

In light of the above discussion, the present application is believed to be in condition for allowance. An early and favorable action to that effect is respectfully requested.

Respectfully submitted,

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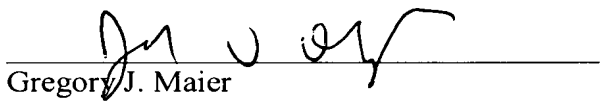

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